Notice of Allowability	Application No.	Applicant(s)	
	09/964,338	HUNT ET AL.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed November 21, 2003*.

2. ☒ The allowed claim(s) is/are *7-16 and 22-30*.

3. ☒ The drawings filed on *28 September 2001* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Gordon Kit on March 11, 2004 and March 16, 2004.

The claims were amended as follows:

Claim 7. A method for the regulated growth of a mammalian host cell in a culture medium, comprising the step of:

Culturing said mammalian host cell in said culture medium, wherein said host cell includes:

(i) at least one introduced DNA sequence encoding a protein, polypeptide and/or peptide factor(s) required for growth of the host cell in said culture medium operably linked to a promoter sequence, the expression of which is regulated by a repressor binding region; and

(ii) at least one introduced DNA sequence encoding a repressor molecule which binds to the repressor binding region, operably linked to an inducible promoter sequence,

wherein cell growth occurs in the absence of an inducer of said inducible promoter and cell growth is inhibited in the presence of an inducer of said inducible promoter.

Claim 22. A **mammalian** host cell including:

(i) at least one introduced DNA sequence encoding a protein, polypeptide and/or peptide factor(s) required for growth of the host cell in a protein/serum-free culture medium operably linked to a promoter sequence, the expression of which is regulated by a repressor binding region; and

(ii) at least one introduced DNA sequence encoding a repressor molecule which binds to the repressor binding region, operably linked to an inducible promoter sequence.

The Examiner acknowledges that acceptance of the above Examiner's Amendment does not mitigate in any way, shape, or form, Applicant's right to pursue additional subject matter in continuation, continuation-in-part, and/or divisional applications pursuant to 35 U.S.C. §§ 120 and 121.

The following is an examiner's statement of reasons for allowance:

The objection to the specification made in the Office Action dated August 21, 2003 is withdrawn in view of the amendments made to the specification in the response dated November 21, 2003. The objection to Figures 3 and 8A is withdrawn because there is nothing in the figures that is essential to understanding the invention.

The rejection of claims 7-16 and 20-30 under 35 U.S.C. 103 is withdrawn in view of Applicant's argument that there no motivation to combine the teachings of Mather et al. and Efrat et al. or Kushner et al.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (571) 272-0886. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RBK
3/11/04

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

EXAMINER'S AMENDMENT B

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Gordon Kit on March 11, 2004 and March 16, 2004.

The claims were amended as follows:

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Claim ~~1~~. A method for the regulated growth of a mammalian host cell in a culture medium, comprising the step of:

Culturing said mammalian host cell in said culture medium, wherein said host cell includes:

(i) at least one introduced DNA sequence encoding a protein, polypeptide and/or peptide factor(s) required for growth of the host cell in said culture medium operably linked to a promoter sequence, the expression of which is regulated by a repressor binding region; and

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(ii) at least one introduced DNA sequence encoding a repressor molecule which binds to the repressor binding region, operably linked to an inducible promoter sequence,

wherein cell growth occurs in the absence of an inducer of said inducible promoter and cell growth is inhibited in the presence of an inducer of said inducible promoter.

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Claim ~~22~~. A **mammalian** host cell including:

(i) at least one introduced DNA sequence encoding a protein, polypeptide and/or peptide factor(s) required for growth of the host cell in a protein/serum-free culture medium operably linked to a promoter sequence, the expression of which is regulated by a repressor binding region; and

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(ii) at least one introduced DNA sequence encoding a repressor molecule which binds to the repressor binding region, operably linked to an inducible promoter sequence.

The Examiner acknowledges that acceptance of the above Examiner's Amendment does not mitigate in any way, shape, or form, Applicant's right to pursue additional subject matter in continuation, continuation-in-part, and/or divisional applications pursuant to 35 U.S.C. §§ 120 and 121.

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1 Claim 7. (Amended) A method for the regulated growth of a mammalian host cell in a culture medium, comprising the step of:

culturing said mammalian host cell in said culture medium, wherein said host cell includes:

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(i) at least one introduced DNA sequence encoding a protein, polypeptide and/or peptide factor(s) required for growth of the host cell in said culture medium operably linked to a promoter sequence, the expression of which is regulated by a repressor binding region; and

(ii) at least one introduced DNA sequence encoding a repressor molecule which binds to the repressor binding region, operably linked to an inducible promoter sequence.

2 25 8. A method according to claim 7, wherein the said repressor binding region is a *lac* operator sequence, and said at least one DNA sequence encoding a repressor molecule encodes a *lac* repressor.

3 9. A method according to claims 7 or 8, wherein the inducible promoter 30 sequence(s) is/are selected from the group consisting of the human metallothionein IIA promoter and the modified human metallothionein IIA promoters. M(1)2 and M(2)6.

4 10. A method according to claim 9, wherein the host cell further includes and expresses a DNA sequence encoding a metallothionein.

5 Claim 11. (Amended) A method according to Claim 10, wherein the DNA sequence(s) encoding the protein, polypeptide and/or peptide growth factor(s) encodes a growth factor(s) selected from the group consisting of insulin, modified insulins, insulin-like growth factors, cytokines, mitogenic proteases and mixtures thereof.

6 12. A method according to claim 11, wherein the DNA sequence(s) encoding the protein, polypeptide and/or peptide growth factor(s) encodes insulin or an insulin-like growth factor.

7 13. A method according to claim 11, wherein the DNA sequence(s) encoding the protein, polypeptide and/or peptide growth factor(s) encode insulin or an insulin-like growth factor, and transferrin.

8 Claim 14. (Amended) A method according to Claim 7, wherein the culture medium is protein/serum-free medium.

9 Claim 15. (Amended) A method according to Claim 7, wherein the mammalian host cell is a Chinese hamster ovary cell.

10 Claim 16. (Amended) A method according to Claim 15, wherein the mammalian host cell is a CHO-K1 cell.

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Claim 22. (Amended) A host cell including:

(i) at least one introduced DNA sequence encoding a protein, polypeptide and/or peptide factor(s) required for growth of the host cell in a protein/serum-free culture medium operably linked to a promoter sequence, the expression of which is regulated by a repressor binding region; and

(ii) at least one introduced DNA sequence encoding a repressor molecule which binds to the repressor binding region, operably linked to an inducible promoter sequence.

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12 23. A host cell according to claim 22, wherein the said repressor binding region is a *lac* operator sequence, and said at least one DNA sequence encoding a repressor molecule encodes a *lac* repressor.

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13 24. A host cell according to claim 22 or 23, wherein the inducible promoter sequence(s) is/are selected from the group consisting of the human metallothionein IIA promoter and the modified human metallothionein IIA promoter, M(1)2 and M(2)6.

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14 25. A host cell according to claim 24, wherein the host cell further includes and expresses a DNA sequence encoding a metallothionein.

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Claim 26. (Amended) A host cell according to Claim 22, wherein the DNA sequence(s) encoding the protein, polypeptide and/or peptide growth factor(s) encodes a growth factor(s) selected from the group consisting of insulin, modified insulins, insulin-like growth factors, cytokines, mitogenic proteases and mixtures thereof.

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16 27. A host cell according to claim 26, wherein the DNA sequence(s) encoding the protein, polypeptide and/or peptide growth factor(s) encodes insulin or an insulin-like growth factor.

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17 28. A host cell according to claim 26, wherein the DNA sequence(s) encoding the protein, polypeptide and/or peptide growth factor(s) encode insulin or an insulin-like growth factor, and transferrin.

18 11

Claim 29. (Amended) A host cell according to Claim 22, wherein the mammalian host cell is a Chinese hamster ovary cell.

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Claim 30. (Amended) A host cell according to Claim 29, wherein the mammalian host cell is a CHO-K1 cell.